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(54) Title: POLYNUCLEOTIDE VACCINE FORMULATIONS

(57) Abstract

The present invention relates to a novel vaccine formulation comprising nucleic acid molecules and a mineral-based adjuvant provided in a biologically effective concentration so as to improve induction of an immune response subsequent to vaccination which correlates to expression of one or more specific antigens encoded by the nucleic acid molecule.

WHAT IS CLAIMED IS:

1. A pharmaceutical formulation, comprising:
(a) a mineral-based, negatively charged adjuvant; and,
(b) a polynucleotide vaccine encoding at least one antigen, such that introduction of said formulation into a vertebrate host results in expression of a biologically effective amount of said antigen or antigens so as to induce a prophylactic or therapeutic immune response.

2. A pharmaceutical formulation of claim 1 wherein said mineral adjuvant is an aluminum phosphate-based adjuvant.

3. A pharmaceutical formulation of claim 2 wherein the molar PO_4/Al ratio of said aluminum phosphate-based adjuvant does not substantially bind to nucleic acid molecules.

4. A pharmaceutical formulation of claim 3 wherein said molar PO_4/Al ratio is about 0.9.

5. A pharmaceutical formulation of claim 3 wherein said aluminum-phosphate based adjuvant is Adju-Phos®.

6. A pharmaceutical formulation of claim 4 wherein said aluminum-phosphate based adjuvant is Adju-Phos®.

7. A pharmaceutical formulation of claim 5 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a disease or disorder selected from the group consisting of human immunodeficiency virus, herpes simplex virus, human influenza, hepatitis A, hepatitis B, hepatitis C, human papilloma virus, tuberculosis, tumor growth, autoimmune disorders and allergies.

8. A pharmaceutical formulation of claim 6 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a disease or disorder selected from the group consisting of human immunodeficiency virus, herpes simplex virus, human influenza, hepatitis A, hepatitis B, hepatitis C, human papilloma virus, tuberculosis, tumor growth, autoimmune disorders and allergies.

9. A pharmaceutical formulation of claim 5 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a veterinary disease or disorder selected from the group consisting of rabies, distemper, foot and mouth disease, anthrax, bovine herpes simplex and bovine tuberculosis.

10. A pharmaceutical formulation of claim 6 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a veterinary disease or disorder selected from the group consisting of rabies, distemper, foot and mouth disease, anthrax, bovine herpes simplex and bovine tuberculosis.

11. A pharmaceutical formulation of claim 7 wherein said polynucleotide vaccine is a DNA plasmid.

12. A pharmaceutical formulation of claim 8 wherein said polynucleotide vaccine is a DNA plasmid.

13. A pharmaceutical formulation of claim 9 wherein said polynucleotide vaccine is a DNA plasmid.

14. A pharmaceutical formulation of claim 10 wherein said polynucleotide vaccine is a DNA plasmid.

15. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 3 into said vertebrate host.

16. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 4 into said vertebrate host.

17. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 5 into said vertebrate host.

18. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 6 into said vertebrate host.

19. The method of claim 15 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of parenteral, inhalation, and oral delivery.

20. The method of claim 16 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of parenteral, inhalation, and oral delivery.

21. The method of claim 17 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of parenteral, inhalation, and oral delivery.

22. The method of claim 18 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of parenteral, inhalation, and oral delivery.

23. The method of claim 19 wherein said method of introduction is intramuscular.

24. The method of claim 20 wherein said method of introduction is intramuscular.

25. The method of claim 21 wherein said method of introduction is intramuscular.

26. The method of claim 22 wherein said method of introduction is intramuscular.

27. A pharmaceutical formulation of claim 1 wherein said mineral adjuvant is a calcium phosphate-based adjuvant.

28. A pharmaceutical formulation of claim 27 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a disease or disorder selected from the group consisting of human immunodeficiency virus, herpes simplex virus, human influenza, hepatitis A, hepatitis B, hepatitis C, human papilloma virus, tuberculosis, tumor growth, autoimmune disorders and allergies.

29. A pharmaceutical formulation of claim 27 wherein said polynucleotide vaccine expresses said antigen or antigens so as to induce a prophylactic or therapeutic immune response against a veterinary disease or disorder selected from the group consisting of rabies, distemper, foot and mouth disease, anthrax, bovine herpes simplex and bovine tuberculosis.

30. A pharmaceutical formulation of claim 28 wherein said polynucleotide vaccine is a DNA plasmid.

31. A pharmaceutical formulation of claim 29 wherein said polynucleotide vaccine is a DNA plasmid.

32. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 27 into said vertebrate host.

33. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 28 into said vertebrate host.

34. A method of inducing an immune response in an vertebrate host which comprises introducing the pharmaceutical formulation of claim 29 into said vertebrate host.

35. The method of claim 32 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of intramuscular, inhalation, and oral delivery.

36. The method of claim 33 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of intramuscular, inhalation, and oral delivery.

37. The method of claim 34 wherein introduction of said pharmaceutical formulation is introduced into said host as selected from the group consisting of intramuscular, inhalation, and oral delivery.

38. The method of claim 35 wherein said method of introduction is intramuscular.

39. The method of claim 36 wherein said method of introduction is intramuscular.

40. The method of claim 37 wherein said method of introduction is intramuscular.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/02414

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A01N 63/00, 65/00, 43/04; A61K 31/70

US CL : 424/, 93.1, 93.6, 93 .7 ; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/, 93.1, 93.6, 93 .7 ; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y, P	US 5,703,057 A (JOHNSTON ET AL.) 30 December 1997, abstract and column 27-30.	1-40
Y	US 5,593,972 A (WEINER ET AL.) 14 January 1997, abstract and columns 21-32.	1-40
Y, P	US 5,703,055 A (FELGNER ET AL.) 30 December 1997, abstract and columns 27-34.	1-40
Y, E	US 5,739,118 A (CARRANO ET AL.) 14 April 1998, abstract and columns 21-25.	1-40

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

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B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS. DIALOG, BIOSIS, SCISEARCH, MEDLINE, EMBASE, JAPIO, CAPLUS
search terms: gene therapy, adjuvants, adjuphos, alum, vector, DNA, HIV, herpes, hepatitus, influenza, papilloma, tuberculosis, tumor growth, autoimmune, allergies, rabies, distemper, foot and mouth, anthrax, plasmid